

## SUPPLEMENTARY MATERIAL

**Supplemental Table S1: Search Strategy**

<b>Database: Cochrane library</b>		
Search no.	Search parameters	Results
1.	exp Coronary Occlusion/	104
2.	(chronic adj2 total adj2 occlusion*).mp.	362
3.	1 or 2	420
4.	exp Percutaneous Coronary Intervention/	5087
5.	percutaneous coronary intervention*.mp.	8996
6.	exp Stents/	3853
7.	stent*.mp.	14170
8.	exp Drug-Eluting Stents/	1249
9.	drug-eluting stent*.mp.	3368
10.	exp Angioplasty/	4326
11.	angioplasty.mp.	8642
12.	or/4-11	23273
13.	3 and 12	350
14.	limit 13 to English language	297
15.	limit 14 to yr="2005 -Current"	275
<b>Database: MEDLINE/Ovid</b>		
Search no.	Search parameters	Results
1.	exp Coronary Occlusion/	2902
2.	(chronic adj2 total adj2 occlusion*).mp.	2934
3.	1 or 2	4762
4.	exp Percutaneous Coronary Intervention/	49113
5.	percutaneous coronary intervention*.mp.	35471
6.	exp Stents/	71705
7.	stent*.mp.	106571
8.	exp Drug-Eluting Stents/	10191
9.	drug-eluting stent*.mp.	14518
10.	exp Angioplasty/	59885
11.	angioplasty.mp.	74272
12.	or/4-11	167656
13.	3 and 12	3103
14.	limit 13 to (English language and humans)	2522
15.	limit 14 to yr="2005 -Current"	2272
<b>Database: Embase</b>		
Search no.	Search parameters	Results
1.	exp Coronary Occlusion/	1876
2.	(chronic adj2 total adj2 occlusion*).mp.	6139
3.	1 or 2	6139
4.	exp Percutaneous Coronary Intervention/	92218
5.	percutaneous coronary intervention*.mp.	75399
6.	exp Stents/	48990
7.	stent*.mp.	192807
8.	exp Drug-Eluting Stents/	30734
9.	drug-eluting stent*.mp.	29821
10.	exp Angioplasty/	85257
11.	angioplasty.mp.	93309
12.	or/4-11	290478
13.	3 and 12	5072
14.	limit 13 to (English language and humans)	4440
15.	limit 14 to yr="2005 -Current"	4161

**Supplemental Table S2: Overview of Included Studies**

Study name (Author name)	Year of publication	Country	Study type and design	Number of patients	Primary outcomes	Secondary outcomes	Follow up duration (median or mean)
<b>Single Arm Studies</b>							
<b>Antegrade Approach</b>							
<b>Chronic total occlusion - percutaneous coronary intervention (CTO-PCI) experience in a single, multi-operator Australian centre: Need for dedicated CTO-PCI programs (BogannaShanmugam et al) (24)</b>	2016	Australia	Retrospective Cohort	82	Procedural success; and In-hospital outcomes including all-cause death, MI and emergency CABG.	Coronary perforation requiring pericardiocentesis or other intervention; stent thrombosis as per Academic Research Consortium (ARC) criteria; bleeding requiring blood product transfusion; stroke; access site vascular complications; and contrast-induced nephropathy.	-
<b>Angiographic predictors of success in antegrade approach (KS et al) (25)</b>	2017	India	Single center retrospective cohort	210	-	-	6 months
<b>Outcomes of percutaneous antegrade intraluminal coronary intervention of chronic total occlusion with remote surgical backup (Akinseye et al) (26)</b>	2018	USA	Retrospective cohort	18	Cardiac death, myocardial infarction, target vessel revascularization, heart failure, stroke, and rehospitalization	-	19.5 months
<b>Retrograde Approach</b>							
<b>The retrograde coronary approach for chronic total occlusions: mid-term results and technical tips &amp; tricks (Sheiban et al) (27)</b>	2007	Italy	Retrospective cohort	18	Wiring, angiographic, and procedural success, long term MACE	-	15 months
<b>European experience with the retrograde approach for the recanalization of coronary artery CTOs; a report on behalf of the EuroCTO club (Sianos et al) (28)</b>	2008	Europe	Prospective cohort	175	-	-	-
<b>Initial Experience of Retrograde Wire Approach</b>	2009	Korea	Single center prospective study	61	-	-	-

<b>in Coronary Chronic Total Occlusion Intervention (Suk et al) (29)</b>							
<b>Retrograde percutaneous recanalization of chronic total occlusion of the coronary (Rathore et al) (30)</b>	2009	Japan	Retrospective Study	157	-	-	-
<b>Retrograde approach for the recanalization of CTO: preliminary experience of a single center (Ge et al) (31)</b>	2010	China	-	42	-	-	30 days
<b>Recanalization strategy of retrograde angioplasty in patients with coronary chronic total occlusion - Analysis of 24 cases, focusing on technical aspects and complications (Lee et al) (32)</b>	2010	Korea	Retrospective cohort	22	-	-	309 days
<b>Retrograde coronary chronic total occlusion revascularization (Karpaliotis et al) (33)</b>	2012	USA	Prospective cohort	462	-	-	-
<b>Efficiency, safety, and long-term follow-up of retrograde approach for CTO recanalization: initial (Belgrade) experience with international proctorship (Stojkovic et al) (34)</b>	2012	Serbia	Retrospective Registry	40	-	-	20 months
<b>Changing strategies of the retrograde approach for chronic total occlusion during the past 7 years (Muramatsu et al) (35)</b>	2013	Japan	Retrospective cohort	281	Success rate and outcomes	-	-
<b>Retrograde approach for the recanalization of coronary chronic total occlusion: collateral selection and collateral related complication (Ma et al) (36)</b>	2013	China	-	84	-	-	-
<b>Japanese multicenter registry evaluating the retrograde approach for chronic coronary total occlusion (Tsuchikane et al) (37)</b>	2013	Japan	Multicenter retrospective registry	801	-	-	-
<b>Retrograde recanalization of chronic total occlusions in Europe (Galassi et al) (38)</b>	2015	Europe	-	1395	-	-	24.7 months

<b>Retrograde chronic total occlusion percutaneous coronary intervention through ipsilateral collateral channels (Azzalini et al) (39)</b>	2017	Europe	Retrospective Cohort	126	Success rate, procedural complications, in-hospital outcomes	-	-
<b>Dissection re-entry Approach</b>							
<b>Treating chronic total occlusions using subintimal tracking and re-entry (Colombo et al) (40)</b>	2005	-	-	31	-	-	5.1 months
<b>Comparison between traditional and guide catheter extension reverse controlled antegrade dissection and retrograde tracking: insights from the PROGRESS-CTO registry (Xenogiannis et al) (41)</b>	2019	USA/Europe/Russia	-	467	-	-	-
<b>Asian-Pacific algorithm</b>							
<b>Procedure failure of chronic total occlusion percutaneous coronary intervention in an algorithm driven contemporary Asia-Pacific Chronic Total Occlusion Club (APCTO Club) multicenter (Chan et al) (42)</b>	2019	China, Hong Kong, Korea, Japan, Taiwan, Singapore, New Zealand, Australia	Prospective cohort	485	-	-	-
<b>Hybrid Approach</b>							
<b>The safety and efficacy of the hybrid approach to chronic total occlusions: Insights from a contemporary multicenter US registry (Menon et al) (43)</b>	2013	USA		287	Technical success, procedural complications	-	No long term
<b>Application of the hybrid approach to chronic total occlusions in patients with previous CABG (Christopoulos et al) (44)</b>	2014	USA	-	496	Procedural success, procedural complications	-	No long term
<b>The efficacy and safety of the hybrid approach to coronary chronic total occlusions: insights from a contemporary multicenter US registry and comparison with prior studies (Christopoulos, et al) (45)</b>	2014	USA	Mixed Prospective/Retrospective	497	Procedural success, procedural complications	-	No long term

<b>The efficacy of hybrid percutaneous coronary intervention in chronic total occlusions caused by in stent restenosis (Christopoulos, et al) (46)</b>	2014	USA	Mixed Prospective/Retrosp ective	521	Procedural success, procedural complications	-	No long term
<b>Application of the "hybrid approach" to chronic total occlusion interventions: a detailed procedural analysis (Michael, et al) (47)</b>	2014	USA	Prospective Cohort	73	Procedural success, procedural complications	-	No long term
<b>Dissection and re-entry techniques and longer-term outcomes following successful percutaneous coronary intervention of chronic total occlusion (Rinfret, et al) (48)</b>	2014	Canada	Prospective Cohort	187	Combined incidence of cardiac death, MI, ischemia driven target vessel revascularization, or re-occlusion	Incidence of recurrent residual angina	398 days
<b>Application and outcomes of a hybrid approach to chronic total occlusion percutaneous coronary intervention in a contemporary multicenter US registry (Christopoulos, et al) (49)</b>	2015	USA	Mixed Prospective/Retrosp ective	1019 (1036 CTOs)	Procedural success, procedural complications	-	No long term
<b>Procedural failure of chronic total occlusion percutaneous coronary intervention: Insights from a multicenter US registry (Sapontis, et al) (50)</b>	2015	USA	Mixed Prospective/Retrosp ective	380	Procedural success, procedural complications	-	No long term
<b>Adoption of the hybrid CTO approach by a single non-CTO operator: procedural and clinical outcomes (Vo, et al) (51)</b>	2015	-	Retrospective Cohort	48 (50 CTOs)	Procedural success, procedural complications	-	No long term
<b>Impact of Crossing Strategy on Intermediate Term Outcomes After Chronic Total Occlusion Percutaneous Coronary Intervention (Amsavelu, et al) (52)</b>	2016	USA	Mixed Prospective/Retrosp ective	173	Procedural success, long term complications including incidence of death at various follow up periods	-	36 months
<b>Hybrid approach improves success of chronic total occlusion angioplasty (Wilson, et al) (53)</b>	2016	UK	-	1156	Procedural success, procedural complications, complications on follow up	-	20 days

<b>Further validation of the hybrid algorithm for CTO PCI; difficult lesions, same success (Basir et al) (54)</b>	2017	USA	Prospective Cohort	270 (279 CTOs)	Procedural success	-	No long term
<b>Outcomes of the retrograde approach through epicardial collaterals in chronic total occlusion percutaneous coronary intervention (Benincasa et al) (55)</b>	2017	Italy	Prospective Cohort	75	MACE on follow up	-	433 days
<b>Safety and efficacy of the hybrid approach in coronary chronic total occlusion percutaneous coronary intervention: the hybrid video registry (Daniels et al) (56)</b>	2017	USA/UK	Prospective Cohort?	194	-	-	No long term
<b>Retrograde approach is as effective and safe as antegrade approach in contemporary percutaneous coronary intervention for chronic total occlusion: Taiwan Single Center Registry (Lee et al) (57)</b>	2017	Taiwan	Prospective Cohort	321	Technical success, procedural complications	-	No long term
<b>Early procedural and health status outcomes after chronic total occlusion angioplasty: a report from the OPEN-CTO registry (Outcomes, patient health status, and efficiency in chronic total occlusion hybrid procedures) (Sapontis et al) (58)</b>	2017		Prospective Cohort	1000 (1054 CTOs)	Procedural success, complications on follow up	-	1 month
<b>The outcomes, patient health status, and efficiency in chronic total occlusion hybrid procedures registry: rationale and design (Sapontis et al) (59)</b>	2017	-	Prospective Cohort	1000 (1096 CTOs)	Procedural success, procedural complications	-	No long term
<b>One-year outcomes after successful chronic total occlusion percutaneous coronary intervention (Wilson et al) (60)</b>	2017	UK	-	805	Procedural success, procedural complications, complications on follow up	-	12 months
<b>Assessing the landscape of percutaneous coronary chronic total occlusion treatment in Belgium and</b>	2018	Belgium/Luxembourg	Mixed Prospective/Retrospective	388 (411 CTOs)	Technical success, procedural complications	-	No long term

<b>Luxembourg: the Belgian working group on chronic total occlusions registry (Maeremans et al) (61)</b>							
One-year clinical outcomes of the hybrid CTO revascularization strategy after hospital discharge: A subanalysis of the multicenter RECHARGE registry (Maeremans et al) (62)	2018	Europe	Prospective Cohort	1067 (1253 CTOs)	Technical success, procedural complications, MACE at 1 year	-	12 months
The hybrid approach to chronic total occlusion percutaneous coronary intervention: Update from the PROGRESS CTO registry (Tajti, et al) (63)	2018	USA/Russia/Europe	-	3055 (3122 CTOs)	Procedural success, procedural complications	-	No long term
<b>Unclassified Approach</b>							
Coronary septal collaterals as an access for the retrograde approach in the percutaneous treatment of coronary chronic total occlusions (Surmely, et al) (64)	2007	Japan	Prospective Cohort	21	-	-	No long term
Procedural and in-hospital outcomes after percutaneous coronary intervention for chronic total occlusions of coronary arteries 2002 to 2008. Impact of novel guidewire techniques (Rathore, et al) (65)	2009	Japan	Retrospective Cohort	806 (904 CTOs)	Procedural success, procedural complications	-	No long term
Validation of J-chronic total occlusion score for chronic total occlusion percutaneous coronary intervention in an independent contemporary cohort (Nombela-Franco, et al) (66)	2013	Canada	Prospective Cohort	209	Procedural success, JCTO classification	-	No long term
Long-term clinical and angiographic outcomes of the mini-STAR technique as a bailout strategy for percutaneous coronary intervention of chronic total occlusion (Galassi, et al) (67)	2014	Italy	Retrospective Cohort	100	Procedural success, event free survival	-	2 years

<b>Complications during retrograde approach for chronic coronary total occlusion (Okamura, et al) (68)</b>	2015	Japan	Prospective Cohort	1166	Procedural success, procedural complications	-	No long term
<b>Clinical prediction score for successful retrograde procedure in chronic total occlusion percutaneous coronary intervention (Chai, et al) (69)</b>	2016	China	Retrospective Cohort	223 (228 CTO lesions)	Procedural success, independent predictors of success	-	No long term
<b>Chronic total coronary occlusion: treatment results (Christensen, et al) (70)</b>	2017	Denmark	Retrospective Cohort	503 (594 CTOs)	Procedural success, procedural complications, adverse events at 3 months, CCS/NYHA class assessment at 3 months		3 months
<b>Double Arm Studies</b>							
<b>Antegrade vs Retrograde Approach</b>							
<b>In-hospital outcomes of percutaneous coronary intervention in patients with chronic total occlusion: insights from the ERCTO (European Registry of Chronic Total Occlusion) registry (Galassi et al) (71)</b>	2011	Europe	Multicenter prospective registry	1914	Rate of procedural success	Procedural time, fluoroscopy time, contrast volume load, periprocedural complications (such as coronary perforation, CIN and MI) and in-hospital MACE.	3 years
<b>Long-Term outcomes of successful chronic total occlusion percutaneous coronary interventions using the antegrade and retrograde approach (Michael et al) (72)</b>	2014	USA	Single center retrospective study	193	TLR	All-cause mortality, MI, TVR, non-target vessel revascularization, any revascularization, and CABG.	2 years
<b>Long-term major adverse cardiac and cerebrovascular events (MACCE) rate: Comparison of retrograde and antegrade recanalization of chronic total coronary occlusions (Bijuklic et al) (73)</b>	2016	Germany	Single center prospective registry	396	Long term MACCE	-	2.3 years
<b>Outcomes with the Use of the Retrograde Approach for Coronary Chronic Total Occlusion Interventions in a Contemporary Multicenter US Registry (Karmapaliotis et al) (74)</b>	2016	USA	Multicenter prospective study	1276	-	-	-



Impact of crossing technique on the incidence of periprocedural myocardial infarction during chronic total occlusion percutaneous coronary intervention (Stetler et al) (75)	2016	USA	Single center retrospective study	184	-	-	-
Outcomes of Percutaneous Coronary Interventions for Chronic Total Occlusion Performed by Highly Experienced Japanese Specialists (Suzuki et al) (76)	2017	Japan	Multicenter prospective registry	2596	-	-	-
<b>Antegrade vs unclassified Approach</b>							
Traditional Antegrade Approach Versus Combined Antegrade and Retrograde Approach in the Percutaneous Treatment of Coronary Chronic Total Occlusions (Hsu et al) (77)	2009	Japan	Single center prospective study	96	-	-	6 months
<b>ADR vs non-ADR Approach</b>							
Use of antegrade dissection re-entry in coronary chronic total occlusion percutaneous coronary intervention in a contemporary multicenter registry (Danek et al) (78)	2015	USA	Multicenter prospective study	1288	-	-	-

**Supplemental Table S3: ROBINS-1 Risk of bias assessment**

Study	Bias Due to Confounding	Bias in Selection of Participants	Bias in Classification of Interventions	Bias Due to Deviations from Intended Interventions	Bias Due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of Reported Results	Overall RoB Judgment
<b>Antegrade Approach</b>								
<b>BogannaShanmugam et al (24)</b>	Moderate	Moderate	Low	Low	Moderate	Moderate	Low	Moderate
<b>KS et al (25)</b>	Moderate	Moderate	Low	Low	Low	Low	Low	Low
<b>Akinseye et al (26)</b>	Moderate	Moderate	Low	Moderate	Low	Low	Moderate	Moderate
<b>Retrograde Approach</b>								
<b>Sheiban et al (27)</b>	Moderate	Moderate	Low	Low	Low	Low	Low	Low
<b>Sianos et al (28)</b>	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
<b>Suk et al (29)</b>	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
<b>Rathore et al (30)</b>	Low	Moderate	Moderate	Moderate	Low	Low	Low	Low
<b>Ge et al (31)</b>	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
<b>Lee et al (32)</b>	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
<b>Karpaliotis, et al (33)</b>	Low	Moderate	Moderate	Low	Moderate	Low	Low	Moderate
<b>Stojkovic et al (34)</b>	Low	Moderate	Moderate	Low	Moderate	Low	Low	Moderate
<b>Muramatsu et al (35)</b>	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate
<b>Ma et al (36)</b>	Moderate	Low	Low	Moderate	Low	Low	Low	Moderate
<b>Tsuchikane et al (37)</b>	Low	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
<b>Galassi et al (38)</b>	Low	Moderate	Low	Low	Serious	Low	Low	Moderate
<b>Azzalini et al (39)</b>	Moderate	Low	Low	Low	Low	Low	Low	Moderate
<b>Dissection re-entry Approach</b>								
<b>Colombo et al (40)</b>	Moderate	Moderate	Moderate	Low	Low	Moderate	Low	Moderate
<b>Xenogiannis et al (41)</b>	Moderate	Moderate	Low	Low	Moderate	Moderate	Low	Moderate
<b>Asian-Pacific algorithm</b>								
<b>Chan et al (42)</b>	Moderate	Moderate	Low	Moderate	Low	Low	Moderate	Moderate

Hybrid Approach								
Menon, et al (43)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Christopoulos et al (44)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Christopoulos et a (45)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Christopoulos et al (46)	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate	Moderate
Michael, et al (47)	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Rinfret, et al (48)	Moderate	Low	Moderate	Moderate	Low	Low	Low	Low
Christopoulos, et al (49)	Moderate	Moderate	Moderate	Moderate	Low	Low	Moderate	Moderate
Sapontis, et al (50)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Vo, et al (51)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Amsavelu, et al (52)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Wilson, et al (53)	Low	Moderate	Moderate	Moderate	Low	Low	Low	Low
Basir et al (54)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Benincasa et al (55)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Daniels et al (56)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Lee et al (57)	Moderate	Moderate	Moderate	Moderate	Low	Low	Low	Moderate
Sapontis et al (58)	Low	Moderate	Moderate	Moderate	Low	Low	Low	Low
Sapontis et al (59)	Moderate	Low	Moderate	Moderate	Low	Low	Low	Moderate
Wilson et al (60)	Low	Low	Moderate	Moderate	Low	Low	Low	Low
Maeremans et al (61)	Low	Low	Moderate	Moderate	Low	Low	Low	Low
Maeremans et al (62)	Moderate	Low	Moderate	Moderate	Low	Low	Low	Moderate
Tajti, et al (63)	Moderate	Low	Moderate	Moderate	Low	Low	Low	Moderate
Unclassified Hybrid Approach								
Surmely, et al (64)	Moderate	Serious	Serious	Moderate	Moderate	Low	Low	Serious
Rathore, et al (65)	Low	Moderate	Moderate	Moderate	Low	Low	Low	Low
Nombela-Franco, et al (66)	Low	Moderate	Low	Low	Low	Low	Low	Low

<b>Galassi, et al (67)</b>	Low	Low	Moderate	Moderate	Low	Low	Low	Low
<b>Okamura, et al (68)</b>	Moderate	Moderate	Moderate	Low	Low	Low	Low	Moderate
<b>Chai, et al (69)</b>	Moderate	Low	Low	Low	Low	Low	Low	Low
<b>Christensen, et al (70)</b>	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
<b>Antegrade vs Retrograde Approach</b>								
<b>Galassi et al (71)</b>	Low	Low	Low	Low	Low	Low	Low	Low
<b>Michael et al (72)</b>	Moderate	Moderate	Moderate	Low	Low	Low	Low	Moderate
<b>Bijuklic et al (73)</b>	Moderate	Low	Low	Low	Moderate	Low	Low	Low
<b>Karmapaliotis et al (74)</b>	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
<b>Stetler et al) (75)</b>	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
<b>Suzuki et al) (76)</b>	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
<b>Antegrade vs unclassified Hybrid Approach</b>								
<b>Hsu et al) (77)</b>	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
<b>ADR vs non-ADR Approach</b>								
<b>Danek et al) (78)</b>	Moderate	Moderate	Moderate	Low	Low	Low	Moderate	Moderate



**Supplemental Table S4: Baseline Patient Characteristics and Outcomes for Single Arm Studies**

Antegrade Approach				
Study	BogannaShanmugam et al (24)	Ks et al (25)	Akinseye et al (26)	Total
<b>Patients (n)</b>	82	210	18	310
<b>CTO lesions (n)</b>	82	210	18	310
<b>Characteristics</b>				
Mean age	62.6	56.5	58.1	58.2
Male, n (%)	70 (85.4)	170 (81)	14 (70)	254 (82)
HTN, n (%)	57 (69.5)	110 (52.4)	17 (85)	184 (59.3)
Dyslipidemia, n (%)	55 (67.1)	-	16 (80)	71 (0.7)
Diabetes, n (%)	19 (23.2)	71 (33.8)	9 (45)	99 (32)
Smoking, n (%)	17 (20.7)	99 (47.1)	15 (75)	131 (42)
Previous MI, n (%)	9 (11)	-	5 (25)	14 (0.1)
Previous PCI, n (%)	18 (22)	-	-	18 (22)
Previous CABG, n (%)	5 (6.1)	-	-	5 (6.1)
CKD, n (%)	-	-	0 (0)	0 (0)
<b>Procedural characteristics</b>				
Number of stents (n)	1.6	-	1.8	1.7
J-CTO score	-	-	1.74	1.74
Procedural duration (min)	88.1	-	-	88.1
<b>Outcomes</b>				
Procedural success rate, n (%)	41 (50)	143 (68.1)	17 (85)	201 (65)
Technical success rate, n (%)	-	-	18 (90)	18 (90)
<b>Complications</b>				
Cardiac mortality, n (%)	-	-	0 (0) in hospital	0 (0) in hospital
All-cause mortality, n (%)	1 (1.2) in hospital	0 (0) in hospital 2 (1.2) long term	0 (0) in hospital	1 (0.3) in hospital 2 (1.2) long term
MACE, n (%)	-	-	0 (0) in hospital	0 (0) in hospital
MI, n (%)	8 (9.8) in hospital	10 (4.8) in hospital	0 (0) in hospital	18 (5.8) in hospital
Stroke, n (%)	1 (1.2) in hospital	0 (0) in hospital 2 (1.2) long term	0 (0) in hospital	1 (0.3) in hospital 2 (1.2) long term
Emergent CABG, n (%)	4 (4.9) in hospital	0 (0) in hospital	0 (0) in hospital	4 (4.9) in hospital
TVR, n (%)	-	-	0 (0) in hospital	0 (0) in hospital
TLR, n (%)	-	-	-	-
Stent thrombosis, n (%)	0 (0) in hospital	-	-	0 (0) in hospital
Coronary dissection, n (%)	-	-	2 (10) in hospital	2 (10) in hospital
Coronary perforation, n (%)	6 (7.3) in hospital	17 (8) in hospital	1 (5) in hospital	24 (7.7) in hospital
Tamponade, n (%)	1 (1.2) in hospital	2 (0.95) in hospital	0 (0) in hospital	3 (1) in hospital
Contrast nephropathy, n (%)	4 (4.9) in hospital	-	-	4 (0.04) in hospital
Bleeding, n (%)	0 (0) in hospital	0 (0) in hospital	-	0 (0) in hospital

<b>Vascular access, n (%)</b>	5 (6.1) in hospital	16 (0.95) in hospital	-	21 (7.1) in hospital			
Retrograde Approach							
Study	Sheiban et al (27)	Sianos et al (28)	Suk et al (29)	Rathore et al (30)	Ge et al (31)	Lee et al (32)	Karmaliotis et al (33)
<b>Patients (n)</b>	18	175	28	157	42	22	462
<b>CTO lesions (n)</b>	18	175	28	157	42	22	462
<b>Characteristics</b>							
<b>Mean age</b>	60	61.4	63.4	64.9	62.8	56	65
<b>Male, n (%)</b>	15 (83)	154 (88)	20 (71)	134 (85.4)	41 (98)	17 (77)	389 (84)
<b>HTN, n (%)</b>	12 (66)	121 (69.1)	16 (57.1)	105 (66.9)	29 (69)	15 (68)	425 (92)
<b>Dyslipidemia, n (%)</b>	-	143 (81.7)	6 (21.4)	64 (40.8)	9 (21)	10 (45)	451 (97.6)
<b>Diabetes, n (%)</b>	5 (28)	52 (29.7)	9 (32.1)	58 (36.9)	14 (33)	7 (32)	208 (45)
<b>Smoking, n (%)</b>	-	72 (41.1)	6 (21.4)	52 (33.1)	21 (50)	12 (55)	-
<b>Previous MI, n (%)</b>	13 (72)	68 (38.9)	6 (21.4)	147 (93.6)	23 (55)	-	220 (47.7)
<b>Previous PCI, n (%)</b>	-	43 (24.6)	11 (39.2)	59 (37.6)	-	-	208 (45)
<b>Previous CABG, n (%)</b>	3 (17)	19 (10.9)	0	28 (17.8)	2 (4.8)	0 (0)	231 (50)
<b>CKD, n (%)</b>	-	-	-	-	-	-	-
<b>Procedural characteristics</b>							
<b>Number of stents (n)</b>	-	2.6	-	-	-	-	-
<b>J-CTO score</b>	-	-	-	-	-	-	-
<b>Procedural duration (min)</b>	-	-	-	-	-	-	150
<b>Outcomes</b>							
<b>Procedural success rate, n (%)</b>	12 (67)	146 (83.4)	20 (64.5)	133 (85)	37 (88.1)	21 (88)	367 (79.4)
<b>Technical success rate, n (%)</b>	-	-	-	-	-	-	376 (81.4)
<b>Complications</b>							
<b>Cardiac mortality, n (%)</b>	-	-	-	-	-	-	-
<b>All-cause mortality, n (%)</b>	-	0 (0) in hospital	1 (3.57) in hospital	0 (0) in hospital	0 (0) in hospital	0 (0) in hospital	1 (0.2) in hospital
<b>MACE, n (%)</b>	1 (5.5) in hospital 5 (28) long term	-	-	7 (4.5) in hospital	3 (7.1) in hospital	0 (0) in hospital 2 (18) long term	-
<b>MI, n (%)</b>	1 (5.5) in hospital	7 (4) in hospital	1 (3.6) in hospital	6 (3.8) in hospital	3 (7.1) in hospital	1 (4.5) long term	2 (0.4) in hospital
<b>Stroke, n (%)</b>	-	1 (0.6) in hospital	-	-	-	0 (0) in hospital	1 (0.2) in hospital
<b>Emergent CABG, n (%)</b>	-	0 (0) in hospital	0 (0) in hospital	1 (0.6) in hospital	0 (0) in hospital	0 (0) in hospital	3 (0.6) in hospital
<b>TVR, n (%)</b>	4 (22) long term	-	0 (0) in hospital	-	0 (0) in hospital	1 (4.5) long term	-
<b>TLR, n (%)</b>	-	-	-	-	-	-	-
<b>Stent thrombosis, n (%)</b>	-	-	-	-	0 (0) in hospital	1 (4.5) in hospital	-
<b>Coronary dissection, n (%)</b>	-	2 (1.1) in hospital	3 (10.7) in hospital	15 (9.6) in hospital	1 (2.4) in hospital	3 (13.6) in hospital	2 (0.4) in hospital
<b>Coronary perforation, n (%)</b>	1 (5.5) in hospital	12 (6.9) in hospital	-	6 (3.8) in hospital	1 (2.4) in hospital	5 (22.7) in hospital	6 (1.3) in hospital
<b>Tamponade, n (%)</b>	-	0 (0) in hospital	0 (0) in hospital	1 (0.6) in hospital	1 (2.4) in hospital	1 (4.5) in hospital	4 (0.87) in hospital
<b>Contrast nephropathy, n (%)</b>	-	-	-	-	-	-	-
<b>Bleeding, n (%)</b>	-	-	-	-	-	-	-
<b>Vascular access, n (%)</b>	-	-	-	-	-	-	-
Retrograde Approach (cont'd)							
Study	Stojkovic et al (34)	Muramatsu et al (35)	Ma et al (36)	Tsuchikane et al (37)	Galassi et al (38)	Azzalini et al (39)	Total
<b>Patients (n)</b>	40	281	84	801	1395	126	3631
<b>CTO lesions (n)</b>	40	281	84	801	1395	126	3631

Characteristics							
Mean age	55.4	-	59.6	65.8	62	65.7	63.7
Male, n (%)	34 (85)	-	77 (91.7)	704 (87.9)	1235 (88.5)	113 (90)	2933 (87.5)
HTN, n (%)	30 (75)	-	41 (48.8)	581 (72.5)	1078 (77.3)	105 (84)	2558 (76.4)
Dyslipidemia, n (%)	25 (62.5)	-	16 (19)	541 (67.5)	1101 (78.9)	101 (81)	2467 (74)
Diabetes, n (%)	8 (20)	-	23 (27.4)	350 (43.7)	405 (29)	46 (37)	1185 (35.5)
Smoking, n (%)	30 (75)	-	48 (57.1)	343 (42.8)	808 (57.9)	64 (51)	1456 (51)
Previous MI, n (%)	21 (52.5)	-	36 (42.9)	413 (51.6)	607 (43.5)	61 (48)	1615 (56)
Previous PCI, n (%)	-	-	-	236 (29.5)	780 (55.9)	85 (67)	1422 (45)
Previous CABG, n (%)	3 (7.5)	-	-	123 (15.4)	246 (17.6)	26 (21)	681 (21)
CKD, n (%)	-	-	-	-	-	-	-
Procedural characteristics							
Number of stents (n)	2.9	-	-	-	-	-	2.75
J-CTO score	-	-	-	-	3	2.36	2.95
Procedural duration (min)	-	189.7	-	195.1	156.3	158	168.6
Outcomes							
Procedural success rate, n (%)	35 (87.5)	224 (79.7)	67 (79.8)	570 (71.2)	1060 (75.3)	103 (82)	2795 (77)
Technical success rate (%)	-	-	-	563 (70.3)	1191 (71.2)	110 (87)	2240 (80.5)
Complications							
Cardiac mortality, n (%)	-	-	-	2 (0.2) in hospital	-	-	2 (0.2) in hospital
All-cause mortality, n (%)	0 (0) in-hospital 2 (5) long term	-	0 (0) in hospital	2 (0.2) in hospital	2 (0.1) in hospital	1 (0.8) in hospital	7 (0.3) in hospital 2 (5) long term
MACE, n (%)	2 (5) in-hospital 4 (11) long term	-	21 (25) in hospital	13 (1.6) in hospital	-	-	47 (4) in hospital 11 (14) long term
MI, n (%)	2 (5) in hospital	-	21 (25) in hospital	4 (0.5) in hospital	7 (0.4) in hospital	9 (7.1) in hospital	63 (2) in hospital 1 (4.5) long term
Stroke, n (%)	-	-	-	2 (0.2) in hospital	0 (0) in hospital	0 (0) in hospital	4 (0.1) in hospital
Emergent CABG, n (%)	1 (2.5) in hospital	-	-	2 (0.2) in hospital	2 (0.1) in hospital	0 (0) in hospital	8 (0.2) in hospital
TVR, n (%)	0 (0) in hospital	-	0 (0) in hospital	-	-	-	4 (2) in hospital 1 (4.5) long term l
TLR, n (%)	-	-	-	1 (0.1) in hospital	-	-	1 (0.1) in hospital
Stent thrombosis, n (%)	-	-	-	-	-	0 (0) in hospital	1 (0.5) in hospital
Coronary dissection, n (%)	1 (2.5) in hospital	6 (2.1) in hospital	1 (1.2) in hospital	-	30 (1.9) in hospital	-	64 (2.4) in hospital
Coronary perforation, n (%)	2 (5) in hospital	5 (1.7) in hospital	3 (3.5) in hospital	-	31 (2) in hospital	10 (7.9) in hospital	82 (2.9) in hospital
Tamponade, n (%)	1 (2.5) in hospital	-	1 (1.2) in hospital	3 (0.4)	15 (1.0) in hospital	5 (3.9) in hospital	32 (1) in hospital
Contrast nephropathy, n (%)	-	-	-	-	-	2 (1.6) in hospital	2 (1.6) in hospital
Bleeding, n (%)	-	-	-	-	-	3 (2.4) in hospital	3 (2.4) in hospital
Vascular access, n (%)	-	-	-	-	16 (1.0) in hospital	3 (2.4) in hospital	19 (1.2) in hospital
Dissection Re-entry Approach							
Study	Colombo et al (40)	Xenogiannis et al (41)	Total				
Patients (n)	31	467	498				
CTO lesions (n)	31	467	498				
Characteristics							



Mean age	59.9	64.9	64.5
Male, n (%)	26 (83.9)	409 (87.6)	435 (87.3)
HTN, n (%)	16 (51.6)	420 (90)	436 (87.5)
Dyslipidemia, n (%)	22 (71)	448 (95.9)	470 (94.3)
Diabetes, n (%)	7 (22.5)	198 (42.4)	205 (41.1)
Smoking, n (%)	17 (54.8)	124 (26.6)	141 (28.3)
Previous MI, n (%)	15 (48.4)	225 (48.1)	240 (48.2)
Previous PCI, n (%)	-	326 (69.8)	326 (69.8)
Previous CABG, n (%)	11 (35.5)	-	11 (35.5)
CKD, n (%)	-	-	-
Procedural characteristics			
Number of stents (n)	2.3	3.2	2.75
J-CTO score	-	3.3	3.3
Procedural duration (min)	-	201	201
Outcomes			
Procedural success rate, n (%)	21 (67.7)	436 (93.4)	457 (91.7)
Technical success rate, n (%)	30 (96.8)	462 (98.9)	492 (98.8)
Complications			
Cardiac mortality, n (%)	-	-	-
All-cause mortality, n (%)	0 (0) in-hospital 1 (3.2) long term	8 (1.7) in hospital	8 (1.6) in hospital 1 (3.2) long term
MACE, n (%)	0 (0) long term	30 (6.4) in hospital	30 (6.4) in hospital 0 (0) long term
MI, n (%)	5 (16.1) in hospital	14 (3) in hospital	19 (3.8) in hospital
Stroke, n (%)	-	2 (0.4) in hospital	2 (0.4) in hospital
Emergent CABG, n (%)	0 (0) in hospital	2 (0.4) in hospital	2 (0.4) in hospital
TVR, n (%)	11 (52.4) long term	-	11 (52.4) in hospital
TLR, n (%)	-	-	-
Stent thrombosis, n (%)	1 (3.2) in hospital	-	1 (3.2) in hospital
Coronary dissection, n (%)	2 (6.5) in hospital	9 (1.9) in hospital	11 (2.2) in hospital
Coronary perforation, n (%)	3 (9.7) in hospital	-	3 (9.7) in hospital
Tamponade, n (%)	0 (0) in hospital 1 (3.2) long term	6 (1.3) in hospital	6 (1.2) in hospital 1 (3.2) long term
Contrast nephropathy, n (%)	-	1 (0.2) in hospital	1 (0.2) in hospital
Bleeding, n (%)	-	-	-
Vascular access, n (%)	-	12 (2.6) in hospital	12 (2.6) in hospital
Asian-Pacific Algorithm			
Study	Chan et al (42)		
Patients (n)	485		
CTO lesions (n)	497		
Characteristics			
Mean age	61.4		
Male, n (%)	427 (88.4)		
HTN, n (%)	353 (72.8)		
Dyslipidemia, n (%)	283 (58.4)		
Diabetes, n (%)	166 (34.2)		

Smoking, n (%)	247 (50.9)						
Previous MI, n (%)	162 (33.4)						
Previous PCI, n (%)	308 (63.5)						
Previous CABG, n (%)	29 (6)						
CKD, n (%)	-						
<b>Procedural characteristics</b>							
Number of stents (n)	-						
J-CTO score	2.9						
Procedural duration (min)	100						
<b>Outcomes</b>							
Procedural success rate, n (%)	447 (89.9)						
Technical success rate, n (%)	455 (93.8)						
<b>Complications</b>							
Cardiac mortality, n (%)	-						
All-cause mortality, n (%)	1 (0.2) in hospital						
MACE, n (%)	19 (3.8) in hospital						
MI (%)	17 (3.4) in hospital						
Stroke, n (%)	1 (0.2) in hospital						
Emergent CABG, n (%)	0 in hospital						
TVR, n (%)	-						
TLR, n (%)	-						
Stent thrombosis, n (%)	1 (0.2) in hospital						
Coronary dissection, n (%)	-						
Coronary perforation, n (%)	-						
Tamponade, n (%)	1 (0.2) in hospital						
Contrast nephropathy, n (%)	-						
Bleeding, n (%)	-						
Vascular access, n (%)	-						
<b>Hybrid Approach</b>							
Study	Menon, et al (43)	Christopoulos, et al (44)	Christopoulos, et al (45)	Christopoulos, et al (46)	Micheal, et al (47)	Rinfret, et al (48)	Christopoulos, et al (49)
Patients (n)	287	496	497	521	73	187	1019
CTO lesions (n)	287	496	497	521	73	187	1036
<b>Characteristics</b>							
Mean age	64.4	65.00	64.70	64.70	65.10	65.00	65.00
Male, n (%)	255 (89.00)	432 (87.00)	432 (87.00)	451 (86.56)	73 (100.00)	151 (80.75)	891 (86.00)
HTN, n (%)	-	422 (90.00)	452 (91.00)	472 (90.60)	66 (90.40)	125 (66.84)	932 (90.00)
Dyslipidemia, n (%)	-	471 (95.00)	-	495 (95.00)	65 (89.00)	-	995 (96.00)
Diabetes, n (%)	129 (45.00)	208 (48.00)	209 (42.00)	216 (41.46)	39 (52.80)	64 (34.22)	445 (43.00)
Smoking, n (%)	-	198 (40.00)	199 (40.00)	203 (38.96)	-	-	-
Previous MI, n (%)	-	179 (36.00)	184 (37.00)	200 (38.39)	36 (49.30)	95 (50.80)	435 (42.00)
Previous PCI, n (%)	172 (60.00)	298 (60.00)	303 (61.00)	326 (62.57)	23 (31.50)	121 (64.71)	694 (67.00)
Previous CABG, n (%)	103 (36.00)	176 (35.48)	179 (36.00)	189 (36.28)	22 (30.00)	54 (28.88)	352 (34.00)
CKD, n (%)	-	-	-	-	-	-	-
<b>Procedural characteristics</b>							
Number of stents (n)	-	-	2.60	2.60	-	-	2.50
J-CTO score	-	2.67	2.70	2.70	-	2.07	2.50
Procedural duration (min)	-	-	108.00	-	159.00	-	119.00

Outcomes							
Procedural success rate, n (%)		450 (90.70)	451 (90.70)	468 (89.80)	63 (86.30)	-	932 (90.00)
Technical success rate, n (%)	267 (93.00)	454 (91.50)	455 (91.50)	480 (92.10)	66 (90.40)	191 (90.09) *	940 (90.73)
Complications							
Cardiac Mortality, n (%)	-	-	-	-	-	0 (0.00) long term	-
All-cause mortality, n (%)	2 (0.70) in hospital	2 (0.40) in hospital	2 (0.40) in hospital	2 (0.38) in hospital	-	3 (1.60) long term	3 (0.29) in hospital
MACE, n (%)	-	9 (1.80) in hospital	9 (1.80) in hospital	12 (2.30) in hospital	-	-	-
MI, n (%)	3 (1.05) in hospital	5 (1.01) in hospital	5 (1.00) in hospital	5 (0.96) in hospital	-	4 (2.00) long term	8 (0.77) in hospital
Stroke, n (%)	-	-	0 (0.00) in hospital	-	-	-	1 (0.10) in hospital
Emergent CABG, n (%)	-	-	0 (0.00) in hospital	-	-	-	-
TVR, n (%)	-	1 (0.20) in hospital	1 (0.2) in hospital	-	-	-	2 (0.19) in hospital
TLR, n (%)	-	-	-	-	-	-	-
Stent thrombosis, n (%)	-	-	-	-	1 (1.37) in hospital	-	-
Coronary dissection, n (%)	-	-	12 (2.40) in hospital	-	-	-	-
Coronary perforation, n (%)	-	-	16 (3.20) in hospital	-	-	-	-
Tamponade, n (%)	1 (0.35) in hospital	2 (0.40) in hospital	2 (0.40) in hospital	1 (0.19) in hospital	-	-	5 (0.48) in hospital
Contrast nephropathy, n (%)	-	-	-	-	-	-	-
Bleeding, n (%)	-	-	3 (0.60) in hospital	2 (0.38) in hospital	-	-	6 (0.58) in hospital
Vascular access, n (%)	1 (0.35) in hospital	1 (0.20) in hospital	8 (1.60) in hospital	1 (0.19) in hospital	-	-	15 (1.45) in hospital
Hybrid Approach (cont'd)							
Study	Sapontis, et al (50)	Vo, et al (51)	Amsavelu, et al (52)	Wilson, et al (53)	Basir, et al (54)	Benincasa, et al (55)	Daniels, et al (56)
Patients (n)	380	48	173	1156	270	75	194
CTO lesions (n)	380	50	173	1156	279	75	194
Characteristics							
Mean age	66.00	63.40	64.90	65.20	65.70	61.90	-
Male, n (%)	334 (88.00)	40 (83.33)	170 (98.30)	914 (79.10)	215 (79.80)	71 (94.67)	-
HTN, n (%)	342 (90.00)	17 (35.42)	157 (90.70)	-	236 (87.30)	58 (77.33)	-
Dyslipidemia, n (%)	361 (95.00)	-	161 (93.10)	-	252 (93.30)	65 (86.67)	-
Diabetes, n (%)	163 (43.00)	7 (14.58)	104 (60.10)	287 (24.80)	140 (52.00)	15 (20.00)	-
Smoking, n (%)	-	7 (14.58)	59 (34.10)	-	57 (21.10)	13 (17.33)	-
Previous MI, n (%)	160 (42.00)	13 (27.08)	82 (47.10)	630 (54.50)	107 (39.50)	40 (53.33)	-
Previous PCI, n (%)	243 (64.00)	13 (27.08)	94 (54.30)	-	221 (81.90)	56 (74.67)	-
Previous CABG, n (%)	141 (37.00)	8 (16.67)	52 (30.60)	255 (22.10)	112 (41.50)	21 (28.00)	58 (30.00)
CKD, n (%)	-	-	-	148 (12.80)	-	8 (10.67)	-
Procedural characteristics							
Number of stents (n)	-	3.00	-	-	-	2.20	-
J-CTO score	2.90	-	2.34	2.50	3.20	2.10	2.33
Procedural duration (min)	109.00	146.10	-	108.00	152.00	142.00	82.00
Outcomes							
Procedural success rate, n (%)	345 (91.30)	46 (92.00)	-	-	245 (90.70)	40 (53.00)	184 (95.00)
Technical success rate, n (%)	-	46 (92.00)	173 (100.00)	-	251 (92.80)	42 (56.00)	-
Complications							
Cardiac mortality, n (%)	-	-	-	-	-	0 (0.00) * long term	-

<b>All-cause mortality, n (%)</b>	2 (0.53) in hospital	0 (0.00) in hospital	11 (6.51) long term	0 (0.00) in hospital 3 (0.30) long term	4 (1.50) in hospital	-	0 (0.00) in hospital
<b>MACE, n (%)</b>	10 (2.63) in hospital	-	-	18 (1.56) long term*	12 (4.40) in hospital	2 (3.00) in hospital 6 (8.80) long term*	-
<b>MI, n (%)</b>	4 (1.05) in hospital	0 (0.00) in hospital	18 (10.55) long term	9 (0.80) in hospital	2 (0.70) in hospital	1 (1.50) long term*	-
<b>Stroke, n (%)</b>	0 (0.00) in hospital	0 (0.00) in hospital	-	5 (0.40) in hospital	3 (1.10) in hospital	-	-
<b>Emergent CABG, n (%)</b>	0 (0.00) in hospital	0 (0.00) in hospital	-	0 (0.00) in hospital	2 (0.7) in hospital	-	-
<b>TVR, n (%)</b>	-	-	61 (35.56) * long term	-	-	5 (7.40) long term	-
<b>TLR, n (%)</b>	-	-	61 (35.56) * long term	-	-	-	-
<b>Stent Thrombosis, n (%)</b>	-	0 (0.00) in hospital	-	-	-	-	-
<b>Coronary dissection, n (%)</b>	-	1 (2.00) in hospital	-	-	-	-	-
<b>Coronary perforation, n (%)</b>	13 (3.42) in hospital	2 (4.00) in hospital	-	53 (4.60) in hospital	-	9 (12.00) in hospital	12 (6.00) in hospital
<b>Tamponade, n (%)</b>	4 (1.05) in hospital	0 (0.00) in hospital	-	8 (0.70) in hospital	5 (1.90) in hospital	1 (1.30) in hospital	-
<b>Contrast nephropathy, n (%)</b>	-	0 (0.00) in hospital	-	3 (0.3) in hospital	-	-	-
<b>Bleeding, n (%)</b>	-	1 (2.00) in hospital	-	-	-	-	-
<b>Vascular access, n (%)</b>	-	3 (6.00) in hospital	-	8 (0.70) in hospital	-	-	-
<b>Hybrid Approach (cont'd)</b>							
<b>Study</b>	<b>Lee, et al (57)</b>	<b>Sapontis, et al (58)</b>	<b>Sapontis, et al (59)</b>	<b>Wilson, et al (60)</b>	<b>Maeremans, et al (61)</b>	<b>Maeremans, et al (62)</b>	<b>Tajti, et al (63)</b>
<b>Patients (n)</b>	321	1000	1000	805	388	1067	3055
<b>CTO lesions (n)</b>	321	1054	1096	805	411	1253	3122
<b>Characteristics</b>							
<b>Mean age</b>	63.60	65.40	65.30	65.30	64.00	66.00	64.80
<b>Male, n (%)</b>	277 (86.30)	804 (80.40)	883 (80.57)	636 (79.00)	313 (80.67)	908 (85.10)	2604 (85.25)
<b>HTN, n (%)</b>	273 (85.00)	852 (85.20)	975 (88.96)	564 (70.00)	284 (73.20)	639 (59.89)	2757 (90.26)
<b>Dyslipidemia, n (%)</b>	135 (42.10)	-	1030 (93.98)	547 (68.00)	329 (84.79)	712 (66.73)	2814 (92.11)
<b>Diabetes, n (%)</b>	103 (32.10)	412 (41.20)	442 (40.33)	217 (27.00)	112 (28.87)	272 (25.49)	1314 (43.02)
<b>Smoking, n (%)</b>	93 (29.00)	638 (68.30)	188 (17.15)	137 (17.00)	110 (28.35)	244 (22.87)	795 (26.01)
<b>Previous MI, n (%)</b>	48 (15.00)	484 (48.40)	535 (48.81)	443 (55.00)	147 (37.89)	399 (37.39)	1405 (46.00)
<b>Previous PCI, n (%)</b>	-	-	728 (66.42)	507 (63.00)	195 (50.26)	596 (55.86)	1995 (65.29)
<b>Previous CABG, n (%)</b>	7 (2.20)	365 (36.50)	389 (35.49)	169 (21.00)	48 (14.43)	183 (17.00)	993 (32.49)
<b>CKD, n (%)</b>	-	135 (13.50)	27 (2.46)	113 (14.00)	54 (13.92)	118 (11.06)	-
<b>Procedural characteristics</b>							
<b>Number of stents (n)</b>	-	-	-	2.50	2.00	2.40	2.40
<b>J-CTO score</b>	3.31	2.30-use 1054	-	2.40	2.20	-	2.43
<b>Procedural duration (min)</b>	104.90	120.70	-	107.00	89.00	86.00	123.00
<b>Outcomes</b>							
<b>Procedural success rate, n (%)</b>	-	-	956 (87.20)	-	-	-	2654 (85.00)
<b>Technical success rate, n (%)</b>	311 (96.90)	862 (86.20)	981 (89.50)	839 (90.3) *	338 (82.24)	922 (86.00)	2711 (86.84)
<b>Complications</b>							
<b>Cardiac mortality, n (%)</b>	-	-	-	8 (0.99) long term	1 (0.24) in hospital	14 (1.31) long term	-
<b>All-cause mortality, n (%)</b>	2 (0.62) in hospital	9 (0.90) in hospital	9 (0.82) in hospital	21 (2.61) long term	1 (0.24) in hospital	20 (1.87) long term	27 (0.85) in hospital
<b>MACE, n (%)</b>	2 (0.62) in hospital	70 (7.00) in hospital	38 (3.47) in hospital	14 (1.80) long term	14 (3.40) in hospital	93 (8.70) long term	95 (3.04) in hospital

MI, n (%)	0 (0.00) in hospital	26 (2.60) in hospital	25 (2.28) in hospital	25 (3.11) long term	9 (2.19) in hospital	15 (1.41) long term	34 (1.08) in hospital
Stroke, n (%)	-	0 (0.00) in hospital	1 (0.09) in hospital	-	-	-	8 (0.26) in hospital
Emergent CABG, n (%)	-	7 (0.70) in hospital	4 (0.36) in hospital	-	-	5 (0.47) in hospital	5 (0.16) in hospital
TVR, n (%)	-	-	-	41 (5.09) long term	1 (0.24) in hospital	59 (5.53) long term	-
TLR, n (%)	-	-	-	37 (4.60) long term	-	-	-
Stent thrombosis, n (%)	-	-	-	11 (1.37) long term	-	-	-
Coronary dissection, n (%)	-	-	-	-	1 (0.24) in hospital	-	-
Coronary perforation, n (%)	-	48 (4.8) in hospital	51 (4.65) in hospital	-	2 (0.49) in hospital	-	-
Tamponade, n (%)	6 (1.87) in hospital	-	18 (1.64) in hospital	-	2 (0.49) in hospital	3 (0.28) in hospital	27 (0.85) in hospital
Contrast nephropathy, n (%)	-	8 (0.8) in hospital	-	-	-	7 (0.66) long term	-
Bleeding, n (%)	1 (0.31) in hospital	3 (0.30) in hospital	95 (8.70) in hospital	-	2 (0.49) in hospital	13 (1.22) long term	-
Vascular access, n (%)	-	43 (4.30) in hospital	-	-	-	6 (0.56) long term	-
Hybrid Approach (cont'd)							
Study	Total						
Patients (n)	13012						
CTO lesions (n)	13466						
Characteristics							
Mean age	65.51						
Male, n (%)	10854 (83.94)						
HTN, n (%)	9623 (83.77)						
Dyslipidemia, n (%)	8432 (86.43)						
Diabetes, n (%)	4898 (37.88)						
Smoking, n (%)	2941 (29.97)						
Previous MI, n (%)	5622 (44.46)						
Previous PCI, n (%)	6585 (62.99)						
Previous CABG, n (%)	3876 (29.53)						
CKD, n (%)	603 (10.79)						
Procedural characteristics							
Number of stents (n)	2.43						
J-CTO score	2.51						
Procedural duration (min)	113.09						
Outcomes							
Procedural success rate, n (%)	6834 (87.50)						
Technical success rate, n (%)	10329 (88.77)						
Complications							
Cardiac mortality, n (%)	1 (0.24) in hospital 22 (1.03) long term						
All-cause mortality, n (%)	65 (0.60) in hospital 58 (1.71) long term						
MACE, n (%)	273 (3.33) in hospital 131 (4.22) long term						
MI, n (%)	135 (1.27) in hospital 63 (2.74) long term						

<b>Stroke, n (%)</b>	18 (0.21) in hospital
<b>Emergent CABG, n (%)</b>	23 (0.27) in hospital
<b>TVR, n (%)</b>	5 (0.20) in hospital 166 (7.86) long term
<b>TLR, n (%)</b>	98 (10.02) long term
<b>Stent thrombosis, n (%)</b>	1 (0.81) in hospital 11 (1.37) long term
<b>Coronary dissection, n (%)</b>	14 (1.46) in hospital
<b>Coronary perforation, n (%)</b>	206 (4.24) in hospital
<b>Tamponade, n (%)</b>	85 (0.79) in hospital
<b>Contrast nephropathy, n (%)</b>	11 (0.50) in hospital 7 (0.66) long term
<b>Bleeding, n (%)</b>	113 (2.29) in hospital 13 (1.22) long term
<b>Vascular access, n (%)</b>	80 (1.59) in hospital 6 (0.56) long term

Unclassified Approach							
Study	Surmely, et al (64)	Rathore, et al (65)	Nombela-Franco, et al (66)	Galassi, et al (67)	Okamura, et al (68)	Chai, et al (69)	Christensen, et al (70)
<b>Patients (n)</b>	21	806	209	100	1166	223	503
<b>CTO lesions (n)</b>	21	904	209	100	1166	228	594
<b>Characteristics</b>							
<b>Mean age</b>	65.30	65.49	67.00	61.40	-	59.35	67.00
<b>Male, n (%)</b>	19 (90.48)	748 (82.74)	171 (81.82)	90 (90.00)	1039 (89.11)	211 (94.62)	401 (79.70)
<b>HTN, n (%)</b>	-	562 (62.17)	146 (69.86)	80 (80.00)	852 (73.07)	140 (61.40)	382 (76.00)
<b>Dyslipidemia, n (%)</b>	-	357 (39.49)	185 (88.52)	-	779 (66.81)	-	385 (76.50)
<b>Diabetes, n (%)</b>	-	360 (39.82)	69 (33.01)	21 (21.00)	520 (44.60)	74 (32.46)	121 (24.10)
<b>Smoking, n (%)</b>	-	252 (27.88)	55 (26.32)	52.00	497 (42.62)	84 (36.84)	162 (32.20)
<b>Previous MI, n (%)</b>	-	778 (86.06)	117 (55.98)	47 (47.00)	592 (50.77)	-	162 (32.20)
<b>Previous PCI, n (%)</b>	-	247 (27.32)	137 (65.55)	47 (47.00)	-	-	179 (35.60)
<b>Previous CABG, n (%)</b>	4 (19.05)	114 (12.61)	59 (28.23)	13 (13.00)	181 (15.52)	9 (3.95)	76 (15.10)
<b>CKD, n (%)</b>	-	-	-	-	-	-	-
<b>Procedural characteristics</b>							
<b>Number of stents (n)</b>	-	-	-	3.20	-	-	-
<b>J-CTO score</b>	-	-	1.99	-	-	-	3.00
<b>Procedural duration (min)</b>	-	-	-	132	193	-	-
<b>Outcomes</b>							
<b>Procedural success rate, n (%)</b>	-	780 (86.28)	187 (89.47)	92 (92.00)	985 (84.48)	-	412 (69.38)
<b>Technical success rate, n (%)</b>	18 (85.71)	791 (87.50)	189 (90.40)	-	-	197 (86.40)	-
<b>Complications</b>							
<b>Cardiac Mortality, n (%)</b>	-	-	-	2 (2.10) long term	3 (0.26) in hospital	-	-
<b>All-cause mortality, n (%)</b>	-	5 (0.55) in hospital	2 (0.96) in hospital	2 (2.10) long term	7 (0.60) in hospital	-	2 (0.34) in hospital
<b>MACE, n (%)</b>	-	17 (1.88) in hospital	4 (1.91) in hospital	10 (10.80) long term	18 (1.54) in hospital	-	-

MI, n (%)	0 (0.00) in hospital	27 (2.99) in hospital	-	3 (3.00) in hospital 2 (2.10) long term	6 (0.51) in hospital	-	12 (2.02) in hospital
Stroke, n (%)	-	-	2 (0.96) in hospital	-	1 (0.09) in hospital	-	1 (0.17) in hospital
Emergent CABG, n (%)	0 (0.00) in hospital	2 (0.22) in hospital	1 (0.48) hospital	0 (0.00) in hospital	2 (0.17) in hospital	-	1 (0.17) in hospital
TVR, n (%)	-	-	-	-	-	-	-
TLR, n (%)	-	-	-	6 (6.45) long term	1 (0.09) in hospital	-	-
Stent thrombosis, n (%)	-	-	-	18 (19.35) long term	-	6 (2.63) in hospital	-
Coronary dissection, n (%)	-	135 (14.93) in hospital	-	-	11 (0.94) in hospital	19 (8.33) * in hospital	-
Coronary perforation, n (%)	-	103 (11.39) in hospital	2 (0.96) in hospital	7 (7.00) in hospital	26 (2.23) in hospital	19 (8.33) * in hospital	-
Tamponade, n (%)	-	6 (0.66) in hospital	-	1 (1.00) in hospital	6 (0.51)	4 (1.75) in hospital	7 (1.18) in hospital
Contrast nephropathy, n (%)	-	-	2 (0.96) in hospital	5 (5.00) in hospital	6 (0.51) in hospital	-	4 (0.67) in hospital
Bleeding, n (%)	-	-	-	-	1 (0.1) in hospital	1 (0.54) in hospital	-
Vascular access, n (%)	-	-	0 (0.00) in hospital	-	8 (0.69) in hospital	-	-
Unclassified Approach (cont'd)							
Study	Total						
Patients (n)	3028						
CTO lesions (n)	3222						
Characteristics							
Mean age	65.11						
Male, n (%)	2679 (85.56)						
HTN, n (%)	2162 (69.52)						
Dyslipidemia, n (%)	1706 (61.32)						
Diabetes, n (%)	1165 (37.46)						
Smoking, n (%)	1102 (35.43)						
Previous MI, n (%)	1696 (58.85)						
Previous PCI, n (%)	610 (35.55)						
Previous CABG, n (%)	456 (14.56)						
CKD, n (%)	-						
Procedural characteristics							
Number of stents (n)	3.20						
J-CTO score	2.74						
Procedural duration (min)	188.18						
Outcomes							
Procedural success rate, n (%)	2456 (82.61)						
Technical success rate, n (%)	1195 (87.74)						
Complications							
Cardiac mortality, n (%)	3 (0.26) in hospital 2 (2.10) long term						
All-cause mortality, n (%)	16 (0.56) in hospital 2 (2.10) long term						
MACE, n (%)	39 (1.71) in hospital 10 (10.80) long term						
MI, n (%)	48 (1.72) in hospital						

	2 (2.10) long term
<b>Stroke, n (%)</b>	4 (0.20) in hospital
<b>Emergent CABG, n (%)</b>	6 (0.20) in hospital
<b>TVR, n (%)</b>	-
<b>TLR, n (%)</b>	1 (0.09) in hospital 6 (6.45) long term
<b>Stent thrombosis, n (%)</b>	6 (2.63) in hospital 18 (19.35) long term
<b>Coronary dissection, n (%)</b>	165 (7.18) in hospital
<b>Coronary perforation, n (%)</b>	157 (6.02) in hospital
<b>Tamponade, n (%)</b>	24 (0.80) in hospital
<b>Contrast nephropathy, n (%)</b>	17 (0.82) in hospital
<b>Bleeding, n (%)</b>	2 (0.14) in hospital
<b>Vascular access, n (%)</b>	8 (0.58) in hospital



**Supplemental Table S5: Baseline Patient Characteristics and Outcomes for Double Arm Studies**

Antegrade vs Retrograde Approach									
Study	Galassi et al (71)			Michael et al (72)			Bijuklic et al (73)		
Arms	Antegrade	Retrograde	P-value	Antegrade	Retrograde	P-value	Antegrade	Retrograde	P-value
Patients (n)	1749	234		152	41		325	71	
CTO lesions (n)	1749	234		152	41		325	71	
Characteristics	-	-	-						
Mean age	-	-	-	63.6	63.7	0.958	63.7	61.8	0.15
Male, n (%)	-	-	-	150 (99)	39 (95)	0.087	280 (86.2)	62 (87.3)	0.79
HTN, n (%)	-	-	-	132 (87)	36 (88)	0.966	322 (99.1)	70 (98.6)	0.71
Dyslipidemia, n (%)	-	-	-	135 (89)	40 (97)	0.088	283 (87.1)	68 (95.8)	0.036
Diabetes, n (%)	-	-	-	64 (42.2)	17 (42.5)	0.980	87 (26.8)	13 (18.3)	0.14
Smoking, n (%)	-	-	-	-	-		-	-	
Previous MI, n (%)	-	-	-	67 (44)	20 (49)	0.592	88 (27.1)	22 (30.9)	0.51
Previous PCI, n (%)	-	-	-	22 (14.6)	16 (39)	0.030	274 (84.3)	66 (92.9)	0.06
Previous CABG, n (%)	-	-	-	28 (18.2)	11 (27.5)	0.208	63 (19.4)	23 (32.4)	0.02
CKD, n (%)	-	-	-	-	-	-	-	-	-
Procedural characteristics									
Number of stents (n)	-	-	-	2.7	3.2	0.001	-	-	-
J-CTO score	-	-	-	-	-	-	2.6	3.9	<0.0001
Procedural duration (min)	-	-	-	120	203	<0.001	62.5	107.7	<0.0001
Outcomes									
Procedural success rate, n (%)	1456 (83.2)	151 (64.5)	<0.001	-	27 (65.8)	-	286 (88)	57 (80.3)	0.07
Technical success rate, n (%)	-	-	-	-	-	-	-	-	-
Complications									
Cardiac mortality, n (%)	-	-	-	-	-	-	-	-	-
All-cause mortality, n (%)	6 (0.3) in hospital	1 (0.4) in hospital	0.8	14 (9.4) long term	8 (19.1) long term	0.107	-	-	-
MACE, n (%)	-	-	-	-	-	-	37 (11.4) long term	7 (10.3) long term	NS
MI, n (%)	18 (1) in hospital	5 (2.1) in hospital	0.08	4 (2.8) long term	2 (6.3) long term	0.772	-	-	-
Stroke, n (%)	1 (0.05) in hospital	0 (0) in hospital	0.8	-	-	-	-	-	-
Emergent CABG, n (%)	3 (0.2) in hospital	0 (0) in hospital	0.5	3 (2) long term	3 (8.5) long term	0.112	-	-	-
TVR, n (%)	1 (0.05) in hospital	0 (0) in hospital	0.8	41 (27) long term	18 (45.6) long term	0.009	-	-	-
TLR, n (%)	-	-	-	39 (25.7) long term	18 (45.6) long term	0.006	-	-	-
Stent thrombosis, n (%)	1 (0.05) in hospital	0 (0) in hospital	0.8	-	-	-	-	-	-
Coronary dissection, n (%)	-	-	-	-	-	-	-	-	-
Coronary perforation, n (%)	42 (2.1) in hospital	11 (4.7) in hospital	0.04	-	-	-	-	-	-
Tamponade, n (%)	9 (0.5) in hospital	2 (0.8) in hospital	0.5	-	-	-	-	-	-
Contrast nephropathy, n (%)	15 (0.8) in hospital	3 (1.2) in hospital	0.5	-	-	-	-	-	-
Bleeding, n (%)	-	-	-	-	-	-	-	-	-

Vascular access, n (%)	12 (0.6) in hospital	2 (0.8) in hospital	0.5	-	-	-	-	-	-
Antegrade vs Retrograde Approach (cont'd)									
Study	Karmapaliotis et al (74)			Stetler et al (75)			Suzuki et al (76)		
Arms	Antegrade	Retrograde	P-value	Antegrade	Retrograde	P-value	Antegrade	Retrograde	P-value
Patients (n)	745	531		115	69		1872	724	
CTO lesions (n)	745	431		115	69		1872	724	
Characteristics									
Mean age	65.1	66.1	0.096	64.2	65.8	0.17	66.8	66.9	0.863
Male, n (%)	609 (81.7)	465 (87.5)	0.005	113 (98.2)	68 (98.6)	0.87	1593 (85.1)	640 (88.4)	0.018
HTN, n (%)	669 (89.8)	474 (89.3)	0.776	106 (92)	61 (88.4)	0.42	1460 (78)	585 (80.8)	0.12
Dyslipidemia, n (%)	702 (94.2)	502 (94.5)	0.824	108 (93.8)	64 (92.8)	0.78	1425 (76.1)	594 (82.1)	0.001
Diabetes, n (%)	343 (46)	231 (43.5)	0.386	75 (65.5)	29 (42)	0.00019	841 (44.9)	332 (45.8)	0.35
Smoking, n (%)	221 (29.7)	147 (27.6)	0.407	39 (33.9)	27 (38.8)	0.51	1086 (58)	451 (62.3)	0.057
Previous MI, n (%)	295 (39.6)	237 (44.6)	0.077	45 (38.7)	40 (58.8)	0.0089	968 (51.7)	371 (51.3)	0.895
Previous PCI, n (%)	453 (60.8)	374 (70.4)	<0.001	60 (52.2)	41 (59.4)	0.34	1157 (61.8)	489 (67.5)	0.007
Previous CABG, n (%)	180 (24.1)	253 (47.7)	<0.001	27 (23.9)	29 (42)	0.0101	139 (7.4)	68 (9.4)	0.105
CKD, n (%)	-	-	-	-	-	-	-	-	-
Procedural characteristics									
Number of stents (n)	2.3	2.9	<0.001	-	-	-	-	-	-
J-CTO score	2.1	3.1	<0.001	2.1	3	<0.0001	1.9	2.4	<0.0001
Procedural duration (min)	100	183	<0.001	105	190	<0.0001	143.8	201.5	<0.0001
Outcomes									
Procedural success rate, n (%)	695 (93.3)	435 (81.9)	<0.001	111 (96.5)	57 (82.6)	0.0014	1690 (90.3)	615 (85)	<0.0001
Technical success rate, n (%)	698 (93.7)	450 (84.8)	<0.001	113 (98.3)	59 (85.5)	0.0007	1703 (91)	632 (87.3)	0.006
Complications									
Cardiac mortality, n (%)	-	-	-	-	-	-	-	-	-
All-cause mortality, n (%)	1 (0.1) in hospital	4 (0.8) in hospital	0.167	-	-	-	4 (0.2) in hospital	3 (0.4) in hospital	0.362
MACE, n (%)	8 (1.1) in hospital	23 (4.3) in hospital	<0.001	2 (1.8) in hospital	3 (4.5) in hospital	0.2853	-	-	-
MI, n (%)	2 (0.3) in hospital	11 (2.1) in hospital	0.003	4 (3.5) in hospital	10 (14.5) in hospital	0.0064	15 (0.8) in hospital	14 (2) in hospital	0.018
Stroke, n (%)	2 (0.3) in hospital	2 (0.4) in hospital	0.999	-	-	-	4 (0.2) in hospital	2 (0.3) in hospital	0.628
Emergent CABG, n (%)	0 (0) in hospital	0 (0) in hospital	-	-	-	-	0 (0) in hospital	0 (0) in hospital	-
TVR, n (%)	-	-	-	-	-	-	-	-	-
TLR, n (%)	-	-	-	-	-	-	-	-	-
Stent thrombosis, n (%)	-	-	-	-	-	-	4 (0.2) in hospital	1 (0.1) in hospital	1
Coronary dissection, n (%)	-	-	-	1 (0.9) in hospital	2 (2.9) in hospital	0.5572	-	-	-
Coronary perforation, n (%)	14 (1.9) in hospital	29 (5.5) in hospital	<0.001	1 (0.9) in hospital	2 (2.9) in hospital	0.5572	4 (0.2) in hospital	7 (0.9) in hospital	<0.0001
Tamponade, n (%)	2 (0.3) in hospital	7 (1.3) in hospital	0.039	1 (0.9) in hospital	1 (1.5) in hospital	0.9999	4 (0.2) in hospital	7 (0.9) in hospital	<0.0001
Contrast nephropathy, n (%)	-	-	-	-	-	-	22 (1.2) in hospital	22 (3.1) in hospital	0.031
Bleeding, n (%)	-	-	-	-	-	-	-	-	-
Vascular access, n (%)	-	-	-	-	-	-	22 (1.2) in hospital	10 (1.4) in hospital	0.844
Antegrade vs Unclassified Approach									
Study	Hsu et al (77)								
Arms	Antegrade	Unclassified Hybrid	P-value						
Patients (n)	59	46							
CTO lesions (n)	69	50							

Characteristics						
Mean age	65.05	65.04	0.998			
Male, n (%)	52 (88.1)	41 (89.1)	0.874			
HTN, n (%)	37 (62.7)	26 (56.5)	0.521			
Dyslipidemia, n (%)	37 (62.7)	34 (73.9)	0.224			
Diabetes, n (%)	29 (49.2)	24 (52.2)	0.759			
Smoking, n (%)	18 (30.5)	14 (30.4)	0.994			
Previous MI, n (%)	13 (22)	17 (37)	0.093			
Previous PCI, n (%)	37 (62.7)	36 (78.3)	0.086			
Previous CABG, n (%)	3 (5.1)	4 (8.7)	0.462			
CKD, n (%)	16 (27.1)	8 (17.4)	0.239			
Procedural characteristics						
Number of stents (n)	1.3	1.8	0.005			
J-CTO score	-	-	-			
Procedural duration (min)	-	-	-			
Outcomes						
Procedural success rate, n (%)	62 (89.9)	40 (80)	0.129			
Technical success rate, n (%)	65 (94.2)	43 (86)	0.127			
Complications						
Cardiac mortality, n (%)	-	-	-			
All-cause mortality, n (%)	0 (0) In-hospital 0 (0) Long term	0 (0) In-hospital 0 (0) Long term	NS NS			
MACE, n (%)	-	-	-			
MI, n (%)	3 (4.3) In-hospital 0 (0) Long term	3 (6) In-hospital 0 (0) Long term	0.684 NS			
Stroke, n (%)	0 (0) In-hospital 0 (0) Long term	0 (0) In-hospital 0 (0) Long term	NS NS			
Emergent CABG, n (%)	-	-	-			
TVR, n (%)	0 (0) In-hospital 6 (16.7) Long term	0 (0) In-hospital 6 (27.3) Long term	NS 0.333			
TLR, n (%)	-	-	-			
Stent thrombosis, n (%)	-	-	-			
Coronary dissection, n (%)	5 (7.2) in hospital	3 (6) in hospital	0.789			
Coronary perforation, n (%)	5 (7.2) in hospital	7 (14) in hospital	0.227			
Tamponade, n (%)	-	-	-			
Contrast nephropathy, n (%)	2 (7.2) in hospital	0 (0) in hospital	0.225			
Bleeding, n (%)	-	-	-			
Vascular access, n (%)	-	-	-			
ADR vs non-ADR Approach						
Study	Danek et al (78)		Danek et al (78)			
Arms	ADR	Non-ADR (AWE + retrograde )	P-value	ADR	AWE only	P-value
Patients (n)	452	836		248	519	
CTO lesions (n)	458	855		248	519	
Characteristics						
Mean age	65.8	65.4	0.48	161 (64.6)	339 (65.4)	0.35
Male, n (%)	398 (88)	685 (82)	0.005	214 (86.4)	411 (79.3)	0.019
HTN, n (%)	409 (90.5)	744 (89)	0.4	227 (91.6)	461 (88.9)	0.25
Dvslipidemia. n (%)	432 (95.5)	782 (93.6)	0.16	236 (95)	487 (93.9)	0.53

<b>Diabetes, n (%)</b>	208 (46.1)	370 (44.3)	0.55	116 (46.7)	236 (45.4)	0.75
<b>Smoking, n (%)</b>	141 (31.3)	232 (27.8)	0.33	80 (32.1)	148 (28.5)	0.002
<b>Previous MI, n (%)</b>	199 (44)	339 (40.6)	0.25	105 (42.3)	202 (38.9)	0.38
<b>Previous PCI, n (%)</b>	294 (65)	542 (64.8)	0.93	157 (63.3)	311 (59.9)	0.37
<b>Previous CABG, n (%)</b>	172 (38)	270 (32.3)	0.04	78 (31.3)	110 (21.1)	0.003
<b>CKD, n (%)</b>	-	-	-	-	-	-
<b>Procedural characteristics</b>						
<b>Number of stents (n)</b>	2.9	2.3	<0.001	2.7	2.1	<0.001
<b>J-CTO score</b>	2.8	2.4	<0.001	2.5	1.9	<0.001
<b>Procedural duration (min)</b>	156.5	111	<0.001	121	87	<0.001
<b>Outcomes</b>						
<b>Procedural success rate, n (%)</b>	389 (85)	775 (90.7)	0.002	228 (91.8)	488 (94.1)	0.23
<b>Technical success rate, n (%)</b>	398 (86.9)	785 (91.8)	0.005	230 (92.7)	489 (94.2)	0.43
<b>Complications</b>						
<b>Cardiac mortality, n (%)</b>	-	-	-	-	-	-
<b>All-cause mortality, n (%)</b>	2 (0.4) in hospital	3 (0.4) in hospital	0.88	1 (0.4) in hospital	0 (0) in hospital	0.32
<b>MACE, n (%)</b>	13 (2.9) in hospital	19 (2.2) in hospital	0.42	5 (2.1) in hospital	3 (0.6) in hospital	0.12
<b>MI, n (%)</b>	4 (0.9) in hospital	9 (1.1) in hospital	0.74	2 (0.8) in hospital	0 (0) in hospital	0.1
<b>Stroke, n (%)</b>	0 (0) in hospital	4 (0.5) in hospital	0.14	0 (0) in hospital	2 (0.4) in hospital	>0.99
<b>Emergent CABG, n (%)</b>	-	-	-	-	-	-
<b>TVR, n (%)</b>	-	-	-	-	-	-
<b>TLR, n (%)</b>	-	-	-	-	-	-
<b>Stent thrombosis, n (%)</b>	-	-	-	-	-	-
<b>Coronary dissection, n (%)</b>	-	-	-	-	-	-
<b>Coronary perforation, n (%)</b>	-	-	-	-	-	-
<b>Tamponade, n (%)</b>	8 (1.8) in hospital	1(0.1) in hospital	<0.001	2 (0.8) in hospital	0 (0) in hospital	0.1
<b>Contrast nephropathy, n (%)</b>	-	-	-	-	-	-
<b>Bleeding, n (%)</b>	-	-	-	-	-	-
<b>Vascular access, n (%)</b>	-	-	-	-	-	-

## **Supplemental Appendix S1. Approaches**

### **Antegrade Approach**

This group includes 3 studies with a total of 310 patients (24-26). Patient demographics, clinical characteristics, and outcomes were reported in [Supplemental Table S4](#). The mean age, calculated using a weighted average, was 58.9 years (range 56.5 – 62.6 years) and the predominant gender was male (82%). In one study where J-CTO score and procedural duration was reported, the average J-CTO score and procedural duration were 1.7 and 88.1 minutes, respectively (26). The mean procedural success rate was 65%. Only one study, performed by Akinseye et al., reported technical success rate of 90% (26). The incidence of peri-procedural all-cause mortality was 0.3%. Akinseye et al. was the only study reported a Cardiac death (0%), MACE (0%), TVR (0%), and coronary dissection (10%) of their study population. Incidence of myocardial infarction was 5.8%. Incidence of in-hospital stroke was 0.3%. Incidence of Coronary perforation and tamponade were 7.7% and 1%, respectively.

### **Retrograde Approach**

13 studies utilizing the retrograde approach were included in this review with a total of 3631 patients (27-39). The mean age was 61.8 years (range 55.4 – 65.8 years) and the predominant gender was male (87.5%). Diabetes, hypertension, previous MI, and previous CABG were prevalent in 35.5%, 76.4%, 56%, and 21% of the total population, respectively. In two studies where J-CTO score was reported, the average J-CTO score, calculated using a weighted average, was 2.68. Five studies reported procedural duration with a weighted mean of 169.8 minutes. The mean procedural success rate was 77%. 4 studies reported technical success (mean 80.5%). Only one study, performed by Tsuchikane et al., reported cardiac death (0.2%). Among the 11 studies

that reported in-hospital all-cause mortality, mean all-cause mortality was 0.3%. The mean of in-hospital MACE among 7 studies was 4%. Incidence of myocardial infarction was 2% and incidence of stroke was 0.1%. In studies that reported the incidence of TVR, coronary dissection, and perforation, the rate was 2%, 2.4%, and 2.9%, respectively. A more detailed presentation of patient demographics, clinical characteristics, and outcomes were reported in [Supplemental Table S4](#).

### **Dissection re-entry Approach**

This group includes 2 studies with a total of 498 patients (40, 41). Patients demographic, clinical characteristics, and outcomes were reported in [Supplemental Table S4](#). The mean age was 62.4 years, and the predominant gender was male (87.3%). In one study where J-CTO score and procedural duration was reported, the mean J-CTO score and procedural duration were 3.3 and 201 minutes, respectively. The mean procedural success rate was 91.7% and technical success rate was 98.8%. The incidence of peri-procedural all-cause mortality was 1.6%. Incidence of peri-procedural MACE was 6.4%, stroke 0.4%, MI 3.8%, coronary dissection 2.3%, and tamponade 1.4%. In the only study that reported TVR, stent thrombosis, and coronary perforation, the rate was 52.4%, 3.2%, and 9.7%, respectively.